

## **Remarks**

### Status of the Application

Claims 1, 2, 4, 7-12, 14-27, 29, and 31-33 were pending in the application at the time the Office Action was mailed. Claims 15-26 and 29 were withdrawn from consideration and claims 3, 5-6, 13, 28 and 30 were canceled. In this amendment claims 1 and 9 have been amended, claims 15-26 and 29 have been canceled, and new claims 34-39 have been added. Accordingly, upon entry of this amendment, claims 1, 2, 4, 7-12, 14, 27, and 31-39 will be pending and before the examiner for consideration.

### Telephonic Interview/Claim 4

Applicants' representative wishes to thank Examiner Chowdhury for the courtesies extended in the May 31, 2007 telephonic interview in which claim 4 was discussed. The Office Action indicated that claim 4 was rejected, but did not provide a basis for the rejection. In the telephonic interview, the examiner indicated that the rejection was mistaken and that claim 4 was allowable.

### Indefiniteness Rejection

Claims 1-2, 7-12, and 31-33 were rejected under 35 U.S.C. §112, 2d ¶ as being indefinite in the recitation of "codon optimized." In particular, the Office Action stated:

Claim 1 is indefinite in the recitation of "codon optimized" which is confusing i.e. codon optimized for what? Codon optimization is a known process for expressing a gene encoding a protein in

increased amount, which is specific for a particular species i.e. codon optimization for human is different from bacteria. It is not clear to the Examiner regarding above phrase whether the codon optimized for human or bacteria or for anything else? Accordingly, claims 2, 7-12 and 31-32 are rejected, as they are dependent on claim 1.

Although applicants do not necessarily agree or acquiesce in this rejection, claims 1 and 9 (which does not depend from claim 1) have herewith been amended to indicate that the subject nucleic acid is codon-optimized for expression in a mammalian cell. In addition, new claim 34 presented herewith indicates that the nucleic acid is codon-optimized for expression in a human cell. Accordingly, withdrawal of this rejection is respectfully requested.

Enablement/Non-statutory Subject Matter Rejections

Claims 9-10, 12, and 14 were rejected under the enablement portion of 35 U.S.C. §112, 1<sup>st</sup> ¶ and also apparently under 35 U.S.C. §101. As to the latter, the Office Action stated:

Claims 9-10 and 14 still read on any cell or any mammalian cell, which encompasses multicellular human being that is non-statutory as well as non-enabled.

The §101 rejection based on non-statutory subject matter is incorrect because the claimed subject matter is directed to a “cell” not a “human being.” It is not the law that something capable of being introduced into a human being (such as a non-naturally occurring genetically modified cell) is non-statutory subject matter. If the law were otherwise, every patent covering anything that is capable of introduction into a human being (e.g., an implantable medical device, a drug, a contrast agent, a nutritional supplement, a hair-coloring dye, an ink for tattoos, or a suppository)

would be invalid. Furthermore, applicants cannot understand the reasoning that claims directed to a cell are non-statutory subject matter because they might be placed in a human subject, whereas the claims directed to a nucleic acid (which were not rejected in this basis; e.g. claim 1), which also might be placed in a human being, are statutory subject matter. As this rejection is clearly incorrect, applicants request its withdrawal. If the rejection is not withdrawn, applicants respectfully request a detailed explanation of the rejection as well as a detailed response to applicants' arguments – particularly with regard to how a cell differs from a non-cellular device or nucleic acid capable of introduction into a human being.

Regarding the enablement rejection, the Office Action argues that “because the specification, while being enabling for an isolated host cell transformed with the recited nucleic acids does not reasonably provide enablement for any cell within a multicellular animal which have been transformed with the recited nucleic acids.” Applicants respectfully disagree with this rejection, but, solely for the purpose of attempting to expedite prosecution of the application, have added new claims 35-39 which recite an “isolated host cell....” in accordance with the examiner’s statement that such claims are enabled.

Regarding the Office Action’s argument that making genetically modified animals is highly unpredictable, the examiner relies on several references that were published many years before the current application’s 2003 filing date (one as far back as 1992!). Given the rapidly advancing field of molecular biology, they are clearly not representative of the state of the art at the time the current application was filed. Accordingly, the Office Action’s reliance of these references as evidence in support the enablement rejection is erroneous.

Moreover, although a genetically modified animal might be encompassed within claims 9-10, 12, and 14, the claims themselves are directed to a cell – not a genetically modified animal. Regarding the “how to make” aspect of the enablement requirement, MPEP 2164.01(b) recites:

As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112. Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1533, 3 USPQ2d 1737, 1743 (Fed. Cir.), cert. denied, 484 U.S. 954 (1987).

As previously argued, the application clearly discloses a number of methods of making the claimed invention. For reasons unclear to the applicants, from the universe of different things that the rejected claims encompass (e.g., a cell in tissue culture, a cell injected into an animal, a cell injected into a blastocyst, a cell placed in an electronic device, or a cell in an artificial organ created *ex vivo* in tissue culture), the Office Action focuses its argument on one thing encompassed by the claims, namely transgenic animals that stably express large quantities of protein from a transgene. As set out in the Spectra-Physics, Inc. case cited above, not every single possible method of making every possible different embodiment encompassed by a claim needs to be explicitly taught in order to meet the enablement requirements of §112. If the law were otherwise, for any art, the burden on the applicant would be impossible to meet because the number of things that could encompassed within any claim is infinite.

Indeed all claim-containing U.S. patents that have ever issued do not and cannot teach anywhere near all of the possible things encompassed by their claims. As an on point

illustration, US patent 5,874,394 (relied on in the Office Action for the §103 rejection) issued with claims 71 and 78 as follows:

71. A recombinant host cell comprising a humanized GFP gene.

78. The recombinant host cell of claim 71, wherein said cell is located within a mammal.

The only animal data presented in this application was the use of an AAV vector expressing GFP to infect a guinea pig retina. No other vectors or nucleic acid delivery methods were used in this model, and no other species of mammal (e.g., humans, dogs, cats, cows, sheep, rabbits, monkeys, etc.) were used. Nonetheless, claims 71 and 78 on their face appear to encompass, among other things, (i) the entire universe of ways that a humanized GFP gene can be introduced into a cell, (ii) any kind of cell harboring a humanized GFP gene, and (iii) any kind of animal having a cell harboring a humanized GFP gene. Accordingly, if these claims of the '394 patent are enabled, then clearly the presently pending claims should also be considered enabled. Therefore, reconsideration and withdrawal of this rejection is requested.

#### Rejections under 35 U.S.C. 103

A. Claims 1-2, 7-12, 27, and 31-33 were rejected under 35 U.S.C. 103(a) as being obvious over Sztitner et al. (J Biol Chem 1990 Sep. 25; 265(27): 16581-7), Mao et al. Zhonghua Zhon Liu Za Zhi, 2001 Sep.; 23(5): 359-62) in view of Zolotukhin et al. (US Patent 5,874,394).

B. Claims 31-32 and 33 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sztitner et al., Mao et al., Zolotukhin et al., Greer et al. (Luminescence 2002 Jan-Feb; 17(1): 43-74, Review), and Lowe et al. (US Patent 6,132,983).

The foregoing rejections are almost identical to the §103 rejections presented in the office action mailed June 20, 2006. In the office action mailed November 30, 2006, the examiner stated that this rejection was withdrawn in view of applicants' amendments and argument. The claims rejected under this section are the same or narrower than the claims examined in the November 30, 2006 office action. The presently pending claims are all patentable over the foregoing combination for the same reasons that successfully overcame the previous §103 rejections (see applicants' September 19, 2006 amendment). Accordingly, applicants believe that these rejections are in error and requests their withdrawal or further clarification of why the withdrawn rejections were re-instated.

Applicants also note that the lux system of the present application is significantly different from the GFP system described in the Zolotukhin et al. patent. Unlike monomeric GFP, the lux enzyme is a heterodimeric protein that needs both lux A and lux B to produce light. Because of the required association with lux B, before the experiments described in the application, it could not reasonably have been predicted that codon-optimizing lux A would produce more light than the wild type version. For example, codon-optimizing lux A could have unfavorably changed the stoichiometric ratio of lux A:lux B so that less light was produced than in the wild type situation.

### Conclusion

The claims presented in this amendment are supported throughout the specification, are patentable over the prior art, and do not add new matter.

A Petition for Extension of Time under 37 CFR 1.136(a) is attached hereto and the Commissioner is hereby authorized to charge the fee for a 3-month extension of time in the amount of \$525.00, any required additional claims fee, as well as any underpayment or credit any overpayment of fees under 37 CFR 1.16 or 1.17 as required by this paper to Deposit Account 50-3110.

The examiner is cordially invited to call the undersigned if clarification is needed on any matter within this response, or if the examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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